PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.: 09/255,331

Filing Date: February 22, 1999

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Group Art Unit: 1614

Examiner: V. Kim

Title: METHODS FOR THE TREATMENT OF APOLIPOPROTEIN E RELATED DISEASES

Attorney Docket: 8740-000001COE

Box Patent Application
Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Please amend the application as follows and consider the remarks set forth below.

IN THE CLAIMS

Please amend Claims 2-7, 9, 17-18, 20-22 and 24 in accordance with the following rewritten claims in clean form. Applicant includes herewith an Attachment for Claim Amendments showing a marked up version of each amended claim.

2. (Amended) A method of preventing toxicity caused by a peptide fragment of apolipoprotein E having a molecular weight of at least 5kD to a cell comprising treating

said cell with a compound, wherein the compound is selected from the group consisting of polyvinyl sulfate, pentosan polysulfate, dextran sulfate, heparan sulfate and mixtures thereof.

3. (Amended) A method of preventing toxicity caused by a peptide fragment of apolipoprotein E having a molecular weight of at least 5kD to a cell comprising treating said cell with a compound, wherein the compound comprises napthalenesulfonic acid covalently bonded to a phenyl or naphthyl group.

4. (Amended) The method of Claim 3, wherein the napthalenesulfonic acid is covalently bonded to a phenyl or naphthyl group through a diazo or amide bond.

5. (Amended) The method of Claim 3, wherein the compound is selected from the group consisting of ponceau S, Evan's blue, suramin sodium, direct blue 15, calconcarboxylic acid, amaranth, trypan blue, congo red, benzopurpurin 4b, Chicago sky blue 6b, sulfonazo III and mixtures thereof.

6. (Amended) A method of preventing toxicity caused by a peptide fragment of apolipoprotein E having a molecular weight of at least 5kD to a cell comprising treating said cell with a compound, wherein the compound comprises a triphenylmethane core modified with at least one sulfate or carboxylate group.

7. (Amended) The method of Claim 6, wherein the compound further comprises a triphenylmethane core modified with at least one benzoic acid or benzenesulfonic acid substituent.

9. (Amended) The method of Claim 6, wherein the compounds are selected from the group consisting of aurintricarboxylic acid, aniline blue, methyl blue, light green SF yellowish, Coomassie brilliant blue G-250, Coomassie brilliant blue R-250, and mixtures thereof.

17. (Amended) A method of treating a mammal having a condition associated with toxicity caused by a peptide fragment of apolipoprotein E having a molecular weight of at least 5kD, comprising administering a composition comprising a pharmacologically effective amount of a compound, wherein the compound is selected from the group consisting of polyvinyl sulfate, pentosan polysulfate, dextran sulfate, heparan sulfate and mixtures thereof.

18. (Amended) A method of treating a mammal having a condition associated with toxicity caused by a peptide fragment of apolipoprotein E having a molecular weight of at least 5kD, comprising administering a composition comprising a pharmacologically effective amount of a compound, wherein the compound comprises napthalenesulfonic acid covalently bonded to a phenyl or naphthyl group.

20. (Amended) The method of Claim 18, wherein the compound is selected from the group consisting of ponceau S, Evan's blue, suramin sulfate, direct blue 15, calconcarboxylic acid, amaranth, trypan blue, congo red, benzopurpurin 4b, Chicago sky blue 6b, sulfonazo III and mixtures thereof.

21. (Amended) A method of treating a mammal having a condition associated with toxicity caused by a peptide fragment of apolipoprotein E having a molecular weight of at least 5kD, comprising administering a composition comprising a pharmacologically effective amount of a compound, wherein the compound comprises a triphenylmethane core modified with at least one sulfate or carboxylate group.

22. (Amended) The method of Claim 21, wherein the compound further comprises a triphenylmethane core modified with at least one benzoic acid or benzenesulfonic acid substituent.

24. (Amended) The method of Claim 21, wherein the compounds are selected from the group consisting of aurintricarboxylic acid, aniline blue, methyl blue,

light green SF yellowish, Coomassie brilliant blue G-250, Coomassie brilliant blue R-250, and mixtures thereof.

Please cancel Claims 1, 10-16 and 25-34.

Please add the following new claims.

35. (New) The method of Claim 17, wherein inhibiting apolipoprotein E toxicity comprises inhibiting binding of apolipoprotein E or fragments of apolipoprotein E to a cell.

36. (New) The method of Claim 35, wherein the fragments of apolipoprotein E comprise residues 141-147 of apolipoprotein E.

37. (New) The method of Claim 17, wherein inhibiting apolipoprotein E toxicity comprises inhibiting production of a peptide fragment of apolipoprotein E comprising residues 141-147 of apolipoprotein E.

38. (New) The method of Claim 17, wherein the condition is selected from the group consisting of Alzheimer's-type senile dementia, a condition associated with cerebral amyloidosis and hyperlupidermia.

39. (New) The method of Claim 17, wherein the condition is selected from the group consisting of coronary heart disease, atherosclerosis, head injury, ischemic stroke, intracerebral hemorrhage, normal pressure hydrocephalus, HIV-associated dementia and HIV-associated peripheral neuropathy.

40. (New) The method of Claim 18, wherein inhibiting apolipoprotein E toxicity comprises inhibiting binding of apolipoprotein E or fragments of apolipoprotein E to a cell.

41. (New) The method of Claim 40, wherein the fragments of apolipoprotein E comprise residues 141-147 of apolipoprotein E.

42. (New) The method of Claim 18, wherein inhibiting apolipoprotein E toxicity comprises inhibiting production of a peptide fragment of apolipoprotein E comprising residues 141-147 of apolipoprotein E.

43. (New) The method of Claim 18, wherein the condition is selected from the group consisting of Alzheimer's-type senile dementia, a condition associated with cerebral amyloidosis and hyperlupidermia.

44. (New) The method of Claim 18, wherein the condition is selected from the group consisting of coronary heart disease, atherosclerosis, head injury, ischemic stroke, intracerebral hemorrhage, normal pressure hydrocephalus, HIV-associated dementia and HIV-associated peripheral neuropathy.

45. (New) The method of Claim 21, wherein inhibiting apolipoprotein E toxicity comprises inhibiting binding of apolipoprotein E or fragments of apolipoprotein E to a cell.

46. (New) The method of Claim 50, wherein the fragments of apolipoprotein E comprise residues 141-147 of apolipoprotein E.

47. (New) The method of Claim 21, wherein inhibiting apolipoprotein E toxicity comprises inhibiting production of a peptide fragment of apolipoprotein E comprising residues 141-147 of apolipoprotein E.

48. (New) The method of Claim 21, wherein the condition is selected from the group consisting of Alzheimer's-type senile dementia, a condition associated with cerebral amyloidosis and hyperlupidermia.

49. (New) The method of Claim 21, wherein the condition is selected from the group consisting of coronary heart disease, atherosclerosis, head injury, ischemic stroke, intracerebral hemorrhage, normal pressure hydrocephalus, HIV-associated dementia and HIV-associated peripheral neuropathy.

REMARKS

Claims 2-9, 17-24 and 35-54 are now pending in the application. The amendments to the claims contained herein are of equivalent scope as originally filed and thus, are not a narrowing amendment.

CONCLUSION

It is believed that the present application is in condition for allowance and such allowance is courteously solicited. Thus, prompt and favorable consideration of this amendment is respectfully requested. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (248) 641-1600.

Respectfully submitted,

Dated: June 27, 2000

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ATTACHMENT FOR CLAIM AMENDMENTS

The following is a marked up version of each amended claim in which underlines indicates insertions and brackets indicate deletions.

2. [The method of Claim 1] A method of preventing toxicity caused by a peptide fragment of apolipoprotein E having a molecular weight of at least 5kD to a cell comprising treating said cell with a compound, wherein the compound is selected from the group consisting of polyvinyl sulfate, pentosan polysulfate, dextran sulfate, heparan sulfate and mixtures thereof.

3. [The method of Claim 1] A method of preventing toxicity caused by a peptide fragment of apolipoprotein E having a molecular weight of at least 5kD to a cell comprising treating said cell with a compound, wherein the compound [further] comprises napthalenesulfonic acid covalently bonded to a phenyl or naphthyl group.

4. The method of Claim [2] 3, wherein the napthalenesulfonic acid is covalently bonded to a phenyl or naphthyl group through a diazo or amide bond.

5. The method of Claim [1] 3, wherein the compound is selected from the group consisting of ponceau S, Evan's blue, suramin sodium, direct blue 15, calconcarboxylic acid, amaranth, trypan blue, congo red, benzopurpurin 4b, Chicago sky blue 6b, sulfonazo III and mixtures thereof.

6. [The method of Claim 1] A method of preventing toxicity caused by a peptide fragment of apolipoprotein E having a molecular weight of at least 5kD to a cell comprising treating said cell with a compound, wherein the compound [further] comprises a triphenylmethane core modified with at least one sulfate or carboxylate group.

7. The method of Claim [1] 6, wherein the compound further comprises a triphenylmethane core modified with at least one benzoic acid or benzenesulfonic acid substituent.

9. The method of Claim [1] 6, wherein the compounds are selected from the group consisting of aurintricarboxylic acid, aniline blue, methyl blue, light green SF yellowish, Coomassie brilliant blue G-250, Coomassie brilliant blue R-250, and mixtures thereof.

17. [The method of Claim 16] A method of treating a mammal having a condition associated with toxicity caused by a peptide fragment of apolipoprotein E having a molecular weight of at least 5kD, comprising administering a composition comprising a pharmacologically effective amount of a compound, wherein the compound is selected from the group consisting of polyvinyl sulfate, pentosan polysulfate, dextran sulfate, heparan sulfate and mixtures thereof.

18. [The method of Claim 16] A method of treating a mammal having a condition associated with toxicity caused by a peptide fragment of apolipoprotein E having a molecular weight of at least 5kD, comprising administering a composition comprising a pharmacologically effective amount of a compound, wherein the compound [further] comprises napthalenesulfonic acid covalently bonded to a phenyl or naphthyl group.

20. The method of Claim [16] 18, wherein the compound is selected from the group consisting of ponceau S, Evan's blue, suramin sulfate, direct blue 15, calconcarboxylic acid, amaranth, trypan blue, congo red, benzopurpurin 4b, Chicago sky blue 6b, sulfonazo III and mixtures thereof.

21. [The method of Claim 16] A method of treating a mammal having a condition associated with toxicity caused by a peptide fragment of apolipoprotein E having a molecular weight of at least 5kD, comprising administering a composition comprising a

pharmacologically effective amount of a compound, wherein the compound [further] comprises a triphenylmethane core modified with at least one sulfate or carboxylate group.

22. The method of Claim [16] 21, wherein the compound further comprises a triphenylmethane core modified with at least one benzoic acid or benzenesulfonic acid substituent.

24. The method of Claim [16] 21, wherein the compounds are selected from the group consisting of aurintricarboxylic acid, aniline blue, methyl blue, light green SF yellowish, Coomassie brilliant blue G-250, Coomassie brilliant blue R-250, and mixtures thereof.